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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/808,146	03/24/2004	Richard C. Durley	PHA-01640/0/US	3007
7590 03/29/2006			EXAMINER	
Pharmacia Corporation Corporate Patent Department P.O. Box 1027 Chesterfield, MO 63006			RAO, DEEPAK R	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 03/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/808,146

Applicant(s)

DURLEY, RICHARD C.

Examiner

Deepak Rao

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 36-38, 50-57 and 71-76 ~~is/are~~ are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 36 and 71-76 ~~is/are~~ are rejected.
- 7) ☒ Claim(s) 37, 38 and 50-57 ~~is/are~~ are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 07192004.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: Notice to comply.

DETAILED ACTION

Claims 36-38, 50-57 and 71-76 are pending in this application.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Particularly, see experimental data in specification page 335, which contains sequences. (See attached notice to comply).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 73-76 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating arthritis, rheumatoid arthritis, asthma or COPD in a subject in need thereof, does not reasonably provide enablement for a method of treating arthritis, rheumatoid arthritis, asthma or COPD in a **subject susceptible to such disorder or condition**. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that “undue experimentation” would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claims recite ‘a method of treating arthritis, rheumatoid arthritis, asthma or COPD in a **subject susceptible to such disorder or condition**’ and the specification fails to enable one skilled in the art for the recited use. There is no disclosure regarding how the ‘subject susceptible to the disorder or condition’ recited in the claim is identified for the treatment. See MPEP § 2164.03 for enablement requirements in cases directed to structure-specific arts such as the pharmaceutical art.

The specification does not provide any guidance regarding how to identify the subject ‘susceptible to the disease’. Test procedure for measuring the inhibition of p38 kinase activity using some of the test compounds are provided in Pages 334-345. There is nothing in the disclosure regarding how this data correlates to identifying ‘a subject susceptible to the conditions’ recited in the claims. The data provided is insufficient such that no reasonable extrapolation could be made by one skilled in the art, between the correlation of the activity of

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the compounds with the identification of the subject. The area of receptor interactions is highly structure specific and unpredictable. Further, there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure for a Markush group.

The instant recitation of 'treating a subject susceptible to such disorder or condition' appears to be directed to 'a method of preventing' the disorder or condition in a subject and therefore, the instant claim language appears to include 'prevention' of the recited disorders in a subject, which is not remotely enabled. 'To prevent' actually means *to anticipate or counter in advance, to keep from happening etc.* (as per Websters II Dictionary) and therefore it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "preventive" effect. It is inconceivable from the *in vitro* data of a small number of representative compounds can be correlated to the 'treatment and prevention' of the conditions recited in the claims, such that the claimed compounds can not only treat but also "prevent" the disorders or conditions of the instant claims. Further, there is no evidence on record which demonstrates that the *in-vitro* screening test relied upon is recognized in the art as being reasonably predictive of success in any of the contemplated areas of 'prevention'. Such a reasonable correlation is necessary to demonstrate such utilities. See *Ex parte Stevens*, 16 USPQ 2d 1379 (BPAI 1990); *Ex parte Busse et al.*, 1 USPQ 2d 1908 (BPAI 1986) (the evidence must be accepted as "showing" such utility, and not "warranting further study").

MPEP § 2164.01(a) states that “A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)”. That conclusion is clearly justified here and undue experimentation will be required to practice the claimed invention.

Thus, factors such as “sufficient working examples”, “the level of skill in the art” and “predictability”, etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Claim 36 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds (of formula depicted in the claim) wherein L and M are independently selected from -O-, -CH₂-, -S-, -N(R)-N(R)-, -C(=O)- or -SO₂- such that each of L and M are different moieties (e.g., L is -O- and M is -CH₂-), does not reasonably provide enablement for compounds wherein both L and M are -O-, -S- (i.e., -O-O-; -S-S-; etc.); or L is -O- and M is -N(R)-N(R)- (i.e., -O-N(R)-N(R)-); etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification fails to enable the preparation of the entire scope of the claimed compounds. The process schemes 1-24 in the specification provide the essential starting materials to prepare the claimed compounds wherein -L-M- is -O-CH₂-, however, there is no disclosure of the sources of starting materials needed to prepare for compounds wherein -L-M- is say -O-O-; -S-S-; -O-N(R)-N(R)-; etc. The specification provides processes of preparing the compounds wherein -L-M- is -O-CH₂-, however, does not provide any explanation or sources such that a person of ordinary skill could determine if a particular group is suitable to be a starting compound for the claimed structural formula. In view of the lack of direction provided in the specification regarding starting materials, the lack of working examples and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention. The starting material sources necessary to obtain the instant compounds must have been available as of the filing date in order to provide an enabling disclosure. See *In re Howarth*, 654 F.2d 103, 210 USPQ 689 (CCPA 1981); *Ex parte Moersch*, 104 USPQ 122 (POBA 1954). Applicants should show that the sources of these starting materials was common knowledge or readily available at the time of filing.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 71-76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. In claim 71, last line recites the term “isomer” which includes all types of isomeric forms including positional isomers which are neither supported in the specification nor shown by examples. Further, there is insufficient antecedent basis for this limitation in claim 38 on which claim 71 is dependent. It is suggested that the last line be replaced with -- or ~~their isomer and~~ pharmaceutically acceptable salt thereof --.
2. Claim 72 recites the limitation "... comprising a compound of claim 71, or a pharmaceutically acceptable salt or **tautomer** thereof" in lines 1-2. There is insufficient antecedent basis for the limitation or a “tautomer” in claims 71 (which depends from claim 38 which depends for claim 36. In the structural formula of claim 36, R₅ is not H and X₁ is not –OH, therefore, it is not clear which of the compounds recited in claim 71 exist in tautomeric form. The discrepancy is found in claims 73-75 also.
3. Claim 72 drawn to a ‘pharmaceutical composition’ does not contain a recitation of -- a pharmaceutically acceptable carrier --.

Allowable Subject Matter

Claims 37-38, and 50-57 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claims 71-72 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims. The closest reference of record, WO 01/29010 does not teach or fairly suggest the instantly claimed compounds.

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Receipt is acknowledged of the Information Disclosure Statement filed on July 19, 2004 and a copy is enclosed herewith.


Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Deepak Rao
Primary Examiner
Art Unit 1624

March 20, 2006

NOTICE TO COMPLY	Application/Control No.	Applicant(s)	
	10/808,146	DURLEY, RICHARD C.	
	Examiner	Art Unit	
	Rao, D.	1624	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☐ 7. Other: .

Applicant Must Provide:

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-2510

For CRF Submission Help, call (571) 272-2501/2583.

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